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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/836,627	04/17/01	COLE	E 6514-11-BHJ

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HM12/0712

EXAMINER

DI NOLA BARON, L

ART UNIT

PAPER NUMBER

1615

DATE MAILED:

07/12/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

09/836,627

Applicant(s)

COLE ET AL.

Examiner

Liliana Di Nola-Baron

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) **SUBSTITUTE**
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 21, 24-27 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention refers to a drug delivery system comprising a HPMC capsule, in which the body and the cap are separately coated or two equal empty HPMC capsule halves are filled with a caplet and separately coated. Additionally, the invention refers to HPMC capsules having a sealing on the gap between the body and the cap. This is in contrast with the written description of the invention, where an overlapping region of capsule body and cap is mentioned (See p.3, line 20). The written description of the coating process claimed in the invention is insufficiently reproducible. The specification lacks direction and guidance regarding the claimed coating process and specific embodiments and illustrative examples pertinent to the scope of the invention. Due to the lack of guidance presented in the specification regarding the methodology of the claimed invention and the absence of working examples directed to a method of separately coating the different components of the HPMC capsule, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

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3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The use of a trade name in the claim to identify or describe the copolymer of the claimed invention renders the claim indefinite and constitutes an improper use of the trade name (See MPEP 2173.05). It is suggested that the trade name be removed from the claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-10, 14-16, 19-20 and 28-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Hatano et al.

The claimed invention refers to a drug delivery composition comprising a HPMC capsule provided with a coating for delivering a drug in the small intestine or colon.

Hatano et al. discloses a coated capsule containing an acidic substance, a polymer film and an enteric coating, for medicament delivery to any site between the upper part of the small intestine and the lower part of the large intestine in the digestive tract (See e.g., p.3, lines 7-10). Hatano et al. explains that the enteric coating film protects the pharmaceutical preparation in the stomach and dissolves in the upper part of the small intestine, allowing the digestive juices to gradually

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penetrate and dissolve the acidic substance in the hard capsule. The acidic solution thus formed dissolves the capsule and the medicaments are released (See e.g., p.3, lines 11-19). Hatano et al. teaches that the pharmaceutical agents in the capsule can be selectively released at any desired site between the jejunum and the rectum and that any type of capsule can be used in the invention, including HPMC capsules (See e.g., p. 4, lines 6-20). Hatano et al. teaches that the enteric polymer used for the enteric coating film must be soluble in a pH higher than 5 and includes a cellulose derivative, an acrylic polymer, a maleic copolymer, a polyvinyl derivative, shellac and the like (See e.g., p. 4, lines 46-49). Among the exemplary polymers, Hatano et al. includes HPMCP, methyl acrylate-acrylic acid copolymer, methyl acrylate-methacrylic acid copolymer and PVAP (See e.g. p. 4, lines 50-58 and p. 5, lines 1-9). Cellulose ester, which is mentioned in claim 15 of the present application as a component of the coating, is considered by the examiner for the purpose of the invention as a not critical element, belonging to the general category of cellulose derivatives. Hatano et al. teaches that the amount of the enteric coating film is from 10 to 400% by weight based on the weight of the hard capsule (See e.g., p. 5, lines 41-46), and that the medicament in the capsule is not limited as long as it is orally administerable (See e.g., p. 8, lines 3-9). Hatano et al. teaches that an alcohol may be used as a solvent for the coating solution (See e.g., p. 9, lines 8-11) and that an intermediate layer comprising a medicament and a water-soluble substance can be provided between the low pH-soluble polymer film and the enteric coating film, if desired (See e.g., p.8, lines 38-52). Additionally, Hatano et al. teaches that a sealing means can be provided around a joint of a body and a cap of the hard capsule and explains that the sealing agent can be any substance able to make the capsule's surface smooth at the joint, such as a water-soluble or insoluble polymer, a low pH-soluble or

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enteric polymer, a saccharide or the like (See e.g., p. 9, lines 23-55). The compositions and drug delivery system described by Hatano et al. meet the limitations of claims 1-10, 14, 15-16, 19-20 and 28-30 of the present application, as they contemplate the administration of a drug to the small intestine or colon by a HPMC capsule containing the drug and provided with a coating, as described in the present application. Thus, Hatano et al. anticipates the claimed invention.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claim 18 is rejected under 35 U.S.C. 102(e) as being anticipated by Tanida et al.

The claimed invention refers to a HPMC capsule to which a coating is applied in the range 5-20 mg/cm² of capsule surface for releasing a drug in the colon and/or terminal ileum.

Tanida et al. discloses a double-coated capsule having a HPMC base, for the release of drugs in the lower gastrointestinal tracts, specifically in the colon (See e.g., p.3, lines 18-52). Tanida et al. teaches that examples of the anionic copolymer, which constitutes the outer layer, include a copolymer of methacrylic acid with methyl methacrylate and HPMCP (See e.g., p. 3, lines 26-30). Tanida et al. teaches that the amount of the coating may vary depending upon the size of the capsule and is within a range of 0.08-0.13 mg/mm² (See e.g., p. 4, lines 22-28 and p. 18, claim 6). The capsule composition and drug delivery system described by Tanida et al. meet the limitations of claim 18, as they contemplate a HPMC capsule for the release of drugs in the colon, to which the coating is applied in the amount/surface range described in the present application. Thus, Tanida et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-24 and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hatano et al., as applied to claims 1-10, 14--16, 19-20 and 28-30 above, and further in view of Watts, Tanida et al. and Paulos.

The teachings of Hatano et al. and Tanida et al. regarding HPMC capsules have been summarized above (See 102 (b) rejection of claims 1-10, 14--16, 19-20 and 28-30 and 102 (e) rejection of claim 18). Hatano et al. does not include a redox sensitive material in the coating of the HPMC capsule

Watts discloses a drug delivery composition for delivering a drug to the colonic region, comprising a coated starch capsule containing the drug (See e.g., p.3, lines 25-29). Watts teaches that the coating may be pH-sensitive, redox-sensitive or sensitive to particular enzymes or bacteria, so that the capsules do not release the drug until it is in the colon (See e.g., p. 5, lines 9-14). Watts teaches that preferred coating materials are those which dissolve at a pH of 5 or above, including CAT, HPMCP, PVAP, shellac and cellulose esters, and that especially preferred materials are methylmethacrylates or copolymers of methacrylic acid and methylmethacrylate (See e.g., p. 5, lines 20-30 and p. 6, lines 1-22). Watts explains that, because of the high presence of microbial anaerobic organisms providing reducing conditions in the colonic region, the coating may comprise a redox-sensitive material, such as azopolymers, which

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are broken down enzymatically, or disulphide polymers (See e.g., p. 6, lines 24-30 and p. 7, lines 1-2).

Paulos discloses a method for making and administering a blinded oral dosage form (See e.g., col. 1, lines 7-11), and more specifically, a capsule containing a tableted medication and having an interlocking body portion and cap portion (See e.g., col. 5, lines 58-61). Paulos teaches that tablets of various sizes and shapes may be placed within the cap or body portion of the capsule (See e.g., col. 8, lines 7-18) and that the body and cap portions may be made of enteric materials (See e.g., col. 13, lines 3-19). Additionally, Paulos teaches that the capsules may be coated by a standard tablet coating process (See e.g., col. 13, lines 39-44) and that the method of the invention may include applying one or more coatings on the capsule, either before or after the tablet is placed within the capsule (See e.g., col. 14, lines 26-37).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the drug delivery system disclosed by Hatano et al., by including a redox sensitive material in the coating of the HPMC capsule, as taught by Watts, and applying the suitable coating in the range recommended by Tanida et al., before or after filling the capsule with the caplet, as taught by Paulos. One of ordinary skill in the art would have been motivated to make such a modification to ensure a complete disintegration of the coating in the small intestine or the colon and prevent drug leaking in the stomach. Because of the teachings of Hatano et al., that any kind of medicament can be delivered to any desired site between the upper part of the small intestine and the lower part of the large intestine in the digestive tract, by controlling the amount and the kind of polymers used for the coating of the HPMC capsule, one of ordinary skill in the art would have a reasonable expectation that the HPMC capsule device of

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the present application would successfully deliver drugs to the small intestine or colon.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

July 10, 2001


THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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